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VALUE IN HEALTH

An Empiric Estimate of the Value of Life: Updating the Renal Dialysis Cost-Effectiveness Standard

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ABSTRACT

Objectives: Proposals to make decisions about coverage of new technology by comparing the technology's incremental cost-effectiveness with the traditional benchmark of dialysis imply that the incremental cost-effectiveness ratio of dialysis is seen a proxy for the value of a statistical year of life. The frequently used ratio for dialysis has, however, not been updated to reflect more recently available data on dialysis.

Methods: We developed a computer simulation model for the end-stage renal disease population and compared cost, life expectancy, and quality-adjusted life expectancy of current dialysis practice relative to three less costly alternatives and to no dialysis. We estimated incremental cost-effectiveness ratios for these alternatives relative to the next least costly alternative and no dialysis and analyzed the population distribution of the ratios. Model parameters and costs were estimated using data from the Medicare population and a large integrated health-care delivery system between 1996 and 2003. The sensitivity of results to model assumptions was tested using 38 scenarios of one-way sensitivity analysis, where parameters informing the cost, utility, mortality and morbidity, etc. components of the model were by perturbed +/–50%.

Results: The incremental cost-effectiveness ratio of dialysis of current practice relative to the next least costly alternative is on average $129,090 per quality-adjusted life-year (QALY) ($61,294 per year), but its distribution within the population is wide; the interquartile range is $71,890 per QALY, while the 1st and 99th percentiles are $65,496 and $488,360 per QALY, respectively. Higher incremental cost-effectiveness ratios were associated with older age and more comorbid conditions. Sensitivity to model parameters was comparatively small, with most of the scenarios leading to a change of less than 10% in the ratio.

Conclusions: The value of a statistical year of life implied by dialysis practice currently averages $129,090 per QALY ($61,294 per year), but is distributed widely within the dialysis population. The spread suggests that coverage decisions using dialysis as the benchmark may need to incorporate percentile values (which are higher than the average) to be consistent with the Rawlsian principles of justice of preserving the rights and interests of society's most vulnerable patient groups.

Keywords: computer simulation, cost-effectiveness analysis, quality-adjusted life-years, renal dysfunction, willingness-to-pay.

Introduction

New medical technologies may improve patient outcomes, but generally contribute to rising health expenditures [1,2]. Existing legislation and conventional medical ethics require managed care organizations and public payers to cover new medical technology as long as it is "reasonable and necessary" without consideration of costs [3]. Although the definition of "reasonable and necessary" is left ambiguous, the decisions made by payers are generally based on the strength of clinical evidence supporting the new technology, especially when the technology is very expensive [3]. Nevertheless, recent debate about the cost of the new Medicare prescription drug benefit program (part D) suggests that continuing on the path where coverage decisions are based on clinical evidence alone without consideration of costs may not be feasible in the long-run. The impending change in legislation has led several researchers to argue that coverage decisions should be based on both cost and effectiveness criteria, where new technology with cost-effectiveness ratios below $50,000 to $100,000 per incremental quality-adjusted life-year (QALY) is deemed suitable for coverage, while others with higher ratios are too expensive [4]. The "threshold" of $50,000 to $100,000 is frequently justified based on the cost-effectiveness of dialysis—an admittedly expensive but effective technology that seems to define the boundary of the highest dollar amount to be paid for an improvement in QALYs [5]. Yet, no recent studies have established the cost-effectiveness of dialysis or examined the implications of adopting a dialysis-related threshold as the basis for coverage decisions. In particular, the broader policy implications of using a threshold calculated based on dialysis practice can be controversial, because it is implied that this threshold is a good proxy for the society's valuation of a statistical year of life.

The objectives in this study were to use current dialysis practice and utility estimates to calculate the cost-effectiveness of dialysis and examine how this ratio varies based on changes in practice patterns (especially the timing of initiation of dialysis) and within patient subgroups. These analyses enabled us to develop a range of estimates for the cost-effectiveness of dialysis that could potentially be used as a threshold for coverage decisions. The process also enabled us to demonstrate how the data utilized in the analysis can be used to estimate the value of life and to examine the implications of this estimate on future coverage decisions for expensive medical technologies.

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Methods

Study Design

We developed a computer simulation model for the end-stage renal disease (ESRD) population to examine the incremental cost-effectiveness ratio (ICER) of dialysis relative to a variety of alternatives, including no dialysis and delayed dialysis. The outcomes for the model included: life expectancy, life expectancy adjusted for quality of life, and economic costs (total societal costs in 2003 US$) discounted at a 3% annual rate and represented in net present values. ICER was calculated relative to the hypothetical reference cases of no dialysis or delayed initiation.

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The sensitivity of the results to model assumptions was tested using 38 scenarios of one-way sensitivity analysis to be described in greater detail below.

Data Sources

Model parameters were estimated from the following data sources: The United States Renal Data System (USRDS) provided data on outcomes and costs from more than 500,000 patients initiating dialysis between 1996 and 2003, as well as from 159,616 patients who received a transplant during the same period [6]. Kaiser Permanenente Northern California provided data on disease progression from more than 1.1 million patients with reduced kidney function cared for between 1996 and 2002. Quality of life data were obtained from direct inquiries of utility [7] that differ by kidney function (as measured by the estimated glomerular filtration rate, eGFR), as well as whether the patient required dialysis. Two sets of utility estimates were provided using alternative methods of quality adjustment: the time tradeoff (TTO) and Health Utilities Index Mark 3 (HUI-3) [8]. The midpoint of the estimates was used as baseline. We considered perturbations to the high end (TTO) and low end (HUI-3) in the sensitivity analysis.

The Simulation Model

Details of the simulation model have been previously reported [9]. A *patient generation model* generated a cohort of 1,000,000 patients, and a *patient simulation model* evolved the profile of each patient over time. The *Patient Generation model* generated random patient profiles for each patient in the cohort. The profile included each patient's age, sex, race and ethnicity, blood type (for simulating the time to transplantation), comorbidities (diabetes, atherosclerotic cardiovascular disease, congestive heart failure, and cancer), eGFR, and serum albumin. Each patient's profile was generated by sampling from the empirical distribution of the incident patient population of the USRDS.

The *Patient Simulation model* generated a medical history for each patient by simulating the time between the following events that modified the patient's profile, determined costs, and affected quality of life and survival: 1) eGFR deterioration capturing the gradual loss of kidney function; 2) hospitalization to capture hospital inpatient episodes; 3) transplantation to capture patients receiving a transplant; 4) graft failure indicating return to dialysis; and 5) death. The time between events is assumed to be exponentially distributed time inhomogeneously, and the mean time between events is modified dynamically by changes in patients' attributes. A summary of the cost parameters and utility scores is provided in Table 1 [10,11]. All remaining parameters are summarized in [9].

Because the main objective of the study was to estimate the cost-effectiveness threshold implied by current dialysis practice and extrapolate from it an estimate for the value of life, we simulated a dialysis strategy that reflected current practice, and additional three strategies where patients would start dialysis later than in current practice, i.e., strategies that are likely to be less costly in terms of (remaining) lifetime cost per patient, because patients would now live shorter and spend less time on dialysis, although only simulation would confirm this because there would also be a rise in hospital costs. In the *Current Practice* strategy, dialysis was started according to a regression function capturing the common practice of starting dialysis roughly when a patient's eGFR dropped below 9 mL/min/1.73 m^2. In the three delay strategies—*Current Practice with Slight Delay, Current Practice with Moderate Delay, and Current Practice with Significant Delay*—patients would not be started dialysis until eGFR fell a further 1.5 mL/min/1.73 m^2 plus an additional 0.1, 0.4, or 0.7 mL/min/1.73 m^2 for each 1 point of Charlson morbidity score below 10. Allowing initiation to depend on the Charlson score (higher for patients suffering from greater morbidity) essentially means that healthier patients would start dialysis later. The delay strategies were specified to mimic a clinically plausible range of delays under resource constraints to enable the measurement of the medical "value" of renal dialysis; this is explained in greater depth in the Discussion [12]. We obtained an ICER for each of the strategies by dividing the difference in cost by the difference in QALYs between that strategy *and the next least costly strategy* [13]. The largest of the ICERs thus obtained provided an estimate for the cost-effectiveness threshold implied by current dialysis practice and the implied value of life (more on this in the Discussion).

In addition, we determined whether this threshold of value of life would change depending on subgroup analysis. A sample of 1000 patients was simulated 10,000 times to calculate the ICER for current practice relative to the next least costly strategy for each patient in the cohort. The cohort of 1000 patients was then divided into quintiles of cost-effectiveness, and both the median and average ICERs within each quintile were computed. To determine the relations among demographic factors, comorbid conditions, and cost-effectiveness, we evaluated the distribution of these factors across quintiles of cost-effectiveness. The latter evaluation was performed to determine the population range of cost-effectiveness and the potential role of patient characteristics in determining the difference.

For comparison, we repeated the analysis using less sophisticated strategies, where the delay was uniform across all patients irrespective of the underlying severity by 12, 24, or 48 months.

Sensitivity Analysis

Baseline parameter values of the simulation model were reported in [9]. There are over 130 parameters describing various costs, utility, and hazard submodels within the simulation model. A 38-scenario sensitivity analysis was conducted, where in each scenario, one or a related group of parameters would be perturbed by +/–50% from their baseline values, and the ICER would be recalculated based on new simulation results. The purpose was to evaluate the uncertainty in which parameters might affect the ratio and by how much. The breakdown of the scenarios are: two scenarios for the rate of hospitalization, two

Table 1 Model assumptions about costs and utilities

	Estimate	Source
Cost ($)		
Hospitalization	12,831 (6,416, 19,247)	
Transplantation	81,330 (40,665, 121,995)	
Transplant follow-up	15,735 (7,868, 23,603)	Medicare
Graft failure	29,392 (14,696, 44,088)	
Dialysis, fixed + EPO	153 (77, 230)	
Dialysis, per minute	0.42 (0.21, 0.63)	
Off-transplant quality of life		
$15 \leq GFR \leq 30$	0.700 (0.35, 1.05)	Gorodetskaya et al. [7]
GFR < 15, no dialysis	0.695 (0.348, 1.043)	
Dialysis	0.630 (0.315, 0.945)	
On-transplant quality of life	0.825 (0.413, 1.238)	Laupacis et al. [10], Hornberger et al. [11]
Discount rate	0.03 (0.015, 0.045)	—

Baseline values are followed by perturbation limits used in the sensitivity analysis.
EPO, erythropoietin; GFR, glomerular filtration rate.

Table 2 Summary of scenarios for the sensitivity analysis

Scenario no.	Scenario summary	% change from baseline	Sign
0	Baseline		
1	Transplant rates up	5	–
2	Transplant rates down	10	+
3	Mean time to hospitalization decreased	2	–
4	Mean time to hospitalization increased	2	–
5	Mortality rates up	0	–
6	Mortality rates down	6	–
7	More graft failures	4	+
8	Fewer graft failures	5	–
9	Rapid eGFR decline	2	–
10	Slow eGFR decline	0	+
11	High discount rate	3	+
12	Low discount rate	8	–
13	Dialysis costs up	35	+
14	Dialysis costs down	39	–
15	Cost of hospitalization up	5	–
16	Cost of hospitalization down	3	+
17	Costs of transplant up	6	+
18	Costs of transplant down	4	–
19	On-dialysis utility up	0	–
20	On-dialysis utility down	2	+
21	On-transplant utility up	1	–
22	On-transplant utility down	3	–
23	Effect of combined dialyzed and native clearance on hospitalization amplified	5	–
24	Effect of combined dialyzed and native clearance on hospitalization deamplified	31	+
25	Effect of dialysis frequency on hospitalization amplified	8	–
26	Effect of dialysis frequency on hospitalization deamplified	11	+
27	Effect of dialysis duration on hospitalization amplified	7	–
28	Effect of dialysis duration on hospitalization deamplified	1	–
29	Effect of zero clearance on hospitalization amplified	4	–
30	Effect of zero clearance on hospitalization deamplified	21	+
31	Effect of combined dialyzed and native clearance on mortality amplified	8	–
32	Effect of combined dialyzed and native clearance on mortality deamplified	27	+
33	Effect of dialysis frequency on mortality amplified	0	–
34	Effect of dialysis frequency on mortality deamplified	3	+
35	Effect of dialysis duration on mortality amplified	7	–
36	Effect of dialysis duration on mortality deamplified	4	+
37	Effect of zero clearance on mortality amplified	2	–
38	Effect of zero clearance on mortality deamplified	4	+

eGFR, estimated glomerular filtration rate.

scenarios for the rate of mortality, two scenarios for the rate of eGFR decline, two scenarios for the rate of transplantation, two scenario for the rate of graft failure, eight scenarios for the effect of dialysis on mortality, eight scenarios for the effect of dialysis on hospitalization, four scenarios for health utility, two scenarios for the costs of dialysis, two scenario for the cost of hospital admissions, two scenarios for the costs of transplantation, follow-up, and graft failure, and two scenarios for the discount rate. Baseline values and perturbation limits for some of the parameters are shown in Table 1, while the scenarios are summarized in Table 2.

Results

Cost-Effectiveness of Dialysis for End-Stage Renal Disease

Table 3 presents the outcomes for the different dialysis strategies considered. Relative to No Dialysis, dialysis increased patient life expectancy by an average of 34.11 months (Current Practice). The total lifetime costs increased from $135,076 (No Dialysis) to $281,640 (Current Practice), respectively. The ICERs, which in Table 3 are calculated relative to the next least costly strategy, depended on the timing of initiation: Current

Table 3 Cost-effectiveness of different dialysis strategies

Outcome	No. of dialysis	Current practice with significant delay	Current practice with moderate delay	Current practice with slight delay	Current practice
Mean survival (months)	47.88	50.78	58.05	68.99	81.99
Mean quality-adjusted survival (quality-adjusted life-months)	28.68	30.32	33.68	38.38	44.55
Mean lifetime cost per person ($)	135,076	140,590	168,820	215,260	281,640
Incremental cost-effectiveness ($ per quality-adjusted life-year gained)		40,446	100,717	118,540	129,090
Incremental cost-effectiveness ($ per life-year gained)		22,792	46,594	50,938	61,294
Mean delay by time (months)		24.29	18.69	11.05	
Mean delay by eGFR (ml/minutes/1.73 m^2)		5.75	4.27	2.62	

Each incremental cost-effectiveness ratio is calculated by dividing the cost difference between a strategy and the strategy to its immediate left by the survival difference (in either years or quality-adjusted years) between the same two strategies.
Slight Delay, Moderate Delay, and Significant Delay mean dialysis would not start until (relative to Current Practice) eGFR fell a further 1.5 ml/min/1.73 m^2 plus an additional 0.1, 0.4, or 0.7 ml/min/1.73 m^2 for each 1 point of Charlson morbidity score below 10.
eGFR, estimated glomerular filtration rate.

Table 4 Incremental cost-effectiveness between different pairs of strategies

Cost-effectiveness ratio ($/QALY) for	No dialysis	Current practice with significant delay	Relative to: current practice with moderate delay	Current practice with slight delay	Current practice
No dialysis					110,814
Current practice with significant delay	40,446				129,090
Current practice with moderate delay	80,993	100,717			124,528
Current practice with slight delay	99,189		118,540		118,902
Current practice	110,814			129,090	—

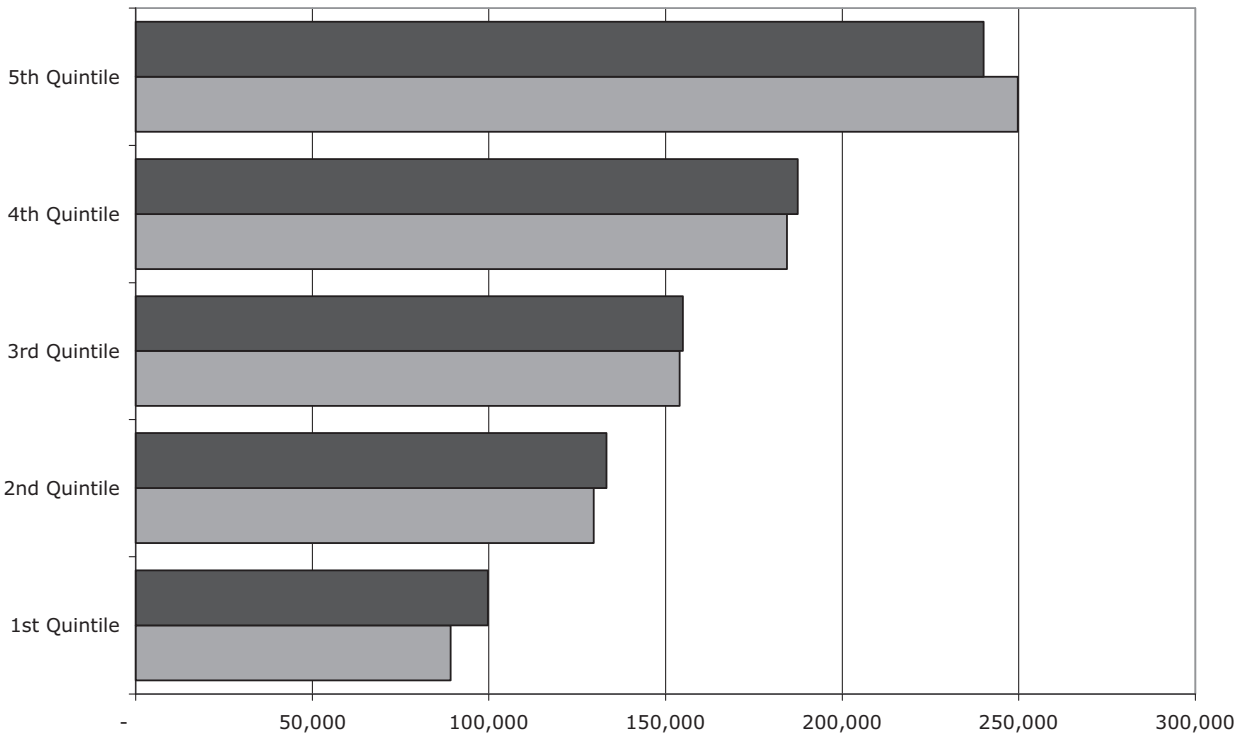
QALY, quality-adjusted life-year.

Practice with Significant Delay had the lowest ICER of $40,446 per QALY, which increased to $129,090 per QALY with Current Practice. When expressed in costs per life-years gained (as opposed to quality adjusted life-years), the ratios ranged from $22,792 to $61,294.

ICERs can also be calculated relative to No Dialysis. Table 4 provides ratios calculated between different pairs of strategies—namely, between each strategy and No Dialysis (first column), between each strategy and Current Practice (last column), and between each strategy and the next least costly strategy (diagonal). In this study, we focus on ratios calculated relative to the next least costly strategy, and a justification for this approach is provided in the Discussion. The most notable figures from this table are $110,814 per QALY for Current Practice relative to No Dialysis, and $129,090 per QALY for Current Practice relative to Current Practice with Slight Delay. These figures can be used to update the frequently cited range of $50,000 to $100,000 per QALY for the incremental cost-effectiveness of dialysis.

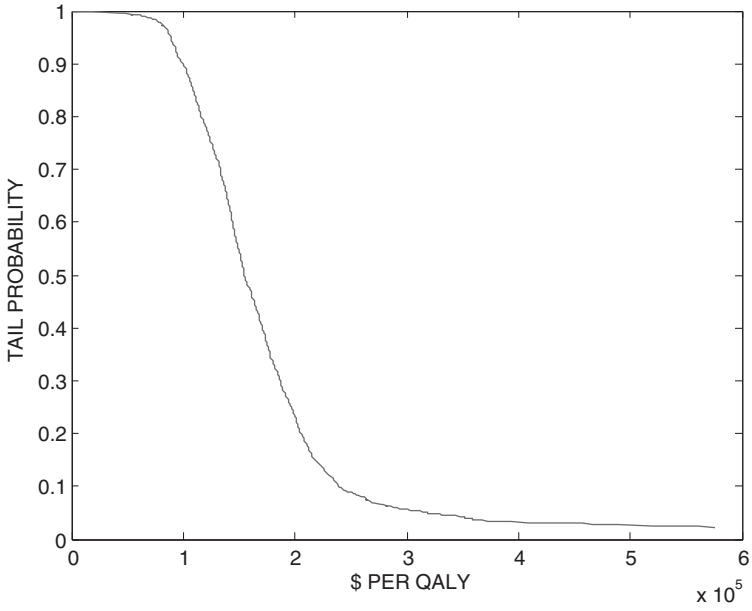
Patient Characteristics and Cost-Effectiveness of Dialysis

The cost-effectiveness of dialysis differed among population subgroups. Figure 1 displays the incremental cost-effectiveness of Current Practice (relative to Current Practice with Slight Delay) with patients ranked into five quintiles. The median ICERs ranged from $99,749 per QALY for the first quintile to $240,010 per QALY for the fifth quintile. Patients in the quintile with the highest ratios were more likely to be older with more comorbid conditions (data not shown). A distribution of the ICER is provided in Figure 2.



	1st Quintile	2nd Quintile	3rd Quintile	4th Quintile	5th Quintile
Median	99,749	133,340	154,840	187,400	240,010
Average	89,150	129,640	153,980	184,330	249,660

Figure 1 Quintiles of the distribution of cost-effectiveness ratios.



	Cumulative Distribution: (100-α)%									
	0.00	**0.01**	**0.02**	**0.03**	**0.04**	**0.05**	**0.06**	**0.07**	**0.08**	**0.09**
0.0	1,304	65,496	77,616	83,800	86,239	88,924	90,838	92,861	94,101	96,621
0.1	99,749	102,320	104,060	106,170	107,760	109,200	110,870	111,940	113,670	114,770
0.2	116,970	118,850	120,880	122,290	123,560	125,280	127,030	128,540	130,100	132,480
0.3	133,340	134,110	135,910	137,260	138,390	139,330	140,180	141,110	142,440	143,490
0.4	144,260	144,820	146,350	147,390	148,230	149,800	150,730	151,820	153,020	153,880
0.5	154,840	156,330	158,170	160,880	161,460	163,590	165,240	166,610	168,160	169,420
0.6	170,590	172,740	173,960	174,990	176,550	177,920	179,810	181,490	183,350	185,680
0.7	187,400	188,140	190,400	192,700	195,040	197,170	198,810	200,850	202,110	203,570
0.8	206,560	207,910	210,850	212,650	214,470	218,750	223,990	226,730	232,330	235,760
0.9	240,010	248,840	261,410	269,340	290,700	319,110	359,260	466,910	477,630	488,360

Figure 2 Tail distribution of the incremental cost-effectiveness ratio for Current Practice (relative to Current Practice with Slight Delay).

Sensitivity Analysis

The last column of Table 2 provides model sensitivity as measured by the absolute percentage change in the ICER (Current Practice relative to Current Practice with Slight Delay) induced by the +/–50% perturbation in the parameters. The sensitivity was comparatively small, with most scenarios leading to a change of no more than 10%. More significant changes were found in scenarios related to changes in the costs of dialysis (13 and 14, at 35% and 39%, respectively) and in the ability of dialysis to attenuate hospitalizations (24 and 30, at 31% and 21%, respectively) and mortality (32, at 27%). Measuring sensitivity using the ICER relative to No Dialysis did not produce an appreciable difference in the pattern or magnitude of sensitivity.

Efficiency Frontier

Figure 3 shows that delay strategies based on the Charlson score dominated the simpler strategies of uniformly delaying all patients by a fixed amount of time. In this article, we focus on ICERs relative to the former set of strategies the rationale for which is discussed below.

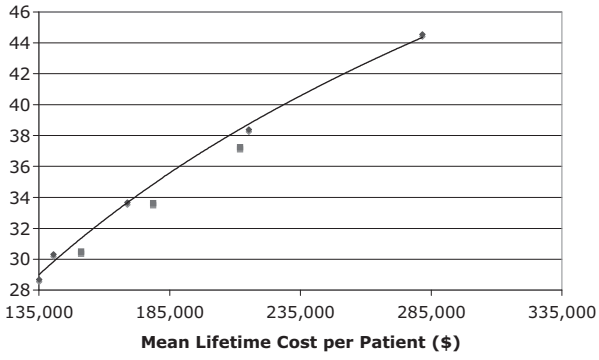


Figure 3 Cost-effectiveness efficiency frontier. The efficiency frontier was obtained by tracing delay strategies based on the Charlson score with a smooth fit. Strategies based on delaying all patients uniformly are found in the interior of the frontier. From left to right, the diamonds correspond to: No Dialysis, Current Practice with Significant Delay, Current Practice with Moderate Delay, Current Practice with Slight Delay, and Current Practice; the squares are: Current Practice with Uniform 48-month Delay, Current Practice with Uniform 24-month Delay, and Current Practice with Uniform 12-month Delay.

Discussion

The cost of dialysis per QALY gained is frequently quoted as a benchmark for the cost-effectiveness of medical technologies.

The most commonly used number is $50,000 per QALY [4], while a more recent study adjusted that number to $93,500 per QALY by inflating the earlier number to 2002 US$ [14]. The original estimate, which can be traced to a 1984 Canadian study, was based on the accounting ledger for 44 dialysis patients at one center during a time span of 1 year and a sophisticated cost-allocation algorithm [5]. Our analysis based on a comprehensive model of the ESRD population and recent data on cost, utility, and disease progression suggests that this benchmark has increased beyond the rate of inflation to exceed the $93,500 per QALY figure: a more accurate figure is between $110,814 per QALY (when Current Practice is compared with No Dialysis) and $129,090 per QALY (when Current Practice is compared to Current Practice with Slight Delay). The increase could be because of the higher than anticipated pace of health expenditure inflation ("price"), or to innovations in nephrology and dialysis care, such as recombinant erythropoietin, available only after the original 1984 estimate ("treatment mix"). The increase might also be simply because of more widespread use of dialysis than before ("technology diffusion"). Alternatively, the utility of patients on dialysis was estimated to be lower than previously utilized values [7].

The frequent use of the cost-effectiveness of dialysis as benchmark, as well as proposals of using it as the threshold for coverage decisions, implies the belief or perception that the cost-effectiveness of dialysis reflects the society's valuation for a statistical year of life. This can be justified based on the economic argument that society's willingness to pay for medical interventions (on a $ per QALY basis) must at least equal the value generated by dialysis for the latter to be universally covered by Medicare, and thus decisions for other medical interventions can be made relative to dialysis. Indeed, the role of dialysis in the history of Medicare is an important and unique one: because Medicare initiated its coverage of ESRD in 1973, dialysis (and more generally renal replacement therapy) has remained the only example where coverage is granted in the United States solely on the basis of a diagnosis [5]. There is also the counterargument that universal coverage for dialysis is an anomaly and hence society's valuation is lower than that implied by dialysis. Irrespectively of one's position on the relevance of dialysis as a benchmark, historical precedence suggests that ICER of dialysis will either approximate society's true valuation of life or provide a useful bound for it. The estimates derived here are consistent with numbers reported elsewhere: The World Health Organization proposes $108,600 per disability-adjusted life-year [15]. When the threshold is expressed in dollars per life-year saved, the estimate derived from dialysis is $61,294 per life-year. This is comparable with the range of $55,000 to $88,000 (2000 US$) reported in [5]. It is also consistent with the average of $65,000 per life-year gained obtained from a survey of health economists and comparable with the range of $44,800 to $83,900 per life-year gained estimated from cardiovascular interventions [13].

The value of a statistical year of life can also be estimated from nonclinical data. A common approach is to calculate the relative increase in salary required for a worker to incur an increase in occupational risk [16]. This method yielded an estimate of $428,286 per QALY in a recent study [17]. Salaries offered to contractors in Iraq, ranging from $60,000 to $175,000 per year, reflect a modern example of the willingness of persons to make economic choices where risks are palpably increased [18]. Assuming an annual risk of death of 0.004 and a salary premium of $30,000 per year over comparable jobs in the United States, and assuming also that dying in Iraq reduces the life expectancy by 30 years, contractors in Iraq are essentially compensated at a rate of $250,000 per statistical year of life. A recent survey of estimates based on occupational risk by Viscusi and Aldy found a range from $500,000 to $21 million per statistical life [19]. Another approach is based on the cost-effectiveness of life-saving interventions in nonmedical fields, such as occupational health, transportation safety, or environmental hazard control [15,16]. Estimates using these methods ranged from $56,000 per life-year saved for transportation programs to $4.2 million per life-year saved for environmental programs [20].

We should provide some justification for the methodologies of using strategies based on delaying dialysis, as well as our calculation of ratios by comparing with the next least costly strategy. In theory, cost-effectiveness analysis (CEA) is a heuristical approximation to an optimal resource allocation problem [21], and the value of the CEA threshold is endogenously determined by the exogenous budget. Most actual applications of CEA reverse this process by directly setting the threshold to avoid the appearance of explicit budget setting [12]. Given its long and unique history of Medicare coverage, dialysis is believed to provide a justifiable benchmark for setting the threshold to, i.e., it represents socially accepted medical "value" ($/QALY). To determine the medical value of dialysis, we assume the level at which dialysis is currently utilized (i.e., Current Practice) derives from a formal decision process. In that decision, physicians could have chosen less dialysis (as represented by Current Practice with Slight Delay), but they did not. That last and most expensive increment of dialysis ($129,090 per QALY) must thus define an implicit value threshold. Although ICERs are more frequently calculated relative to the nonuse of a medical intervention (i.e., No Dialysis), we believe calculating ICERs with respect to a slight delay is reasonable, because the dialysis decision involves a continuous "timing" dimension; indeed, the timing of dialysis is a matter of intense debate in the nephrology community and has spawned policy discussions and recent changes in guidelines [22]. A final point is related to our use of the Charlson score in determining the amount to delay dialysis. The intention here is to better capture how decisions to delay might be carried out in practice: if forced into the situation of having to delay dialysis (because of capacity or budget reasons, for example), physicians would be most reluctant to do so with sicker patients. As a result, we'd expect the sickest patients (i.e., those with the highest Charlson score) to experience the least delay, whereas the healthiest patients would experience the most delay. Another compelling reason is that delaying dialysis by a fixed amount of time uniformly across patients is clinically suboptimal. Figure 3 shows that the strategies of delaying dialysis uniformly across patients by 12, 24, and 48 months are in the interior of the efficiency frontier defined by the delay strategies based on the Charlson score, i.e., they are dominated. Formally optimizing dialysis strategies is beyond the scope of this article and is explored in [23].

The results in Figure 1 show that when distributional considerations are important, making decisions based on the population average of incremental cost-effectiveness ratio as the threshold can be challenging. Consider what would happen if coverage decisions were to be made based on the $129,090 per QALY ($61,294 per year) figure. A straightforward application of this number would imply that a technology would be covered for a population as long as its average cost-effectiveness would be below this figure. Nevertheless, it is possible that this population can be divided into subgroups, with the cost-effectiveness in some subgroups exceeding the threshold, and with some, well below. Providing coverage to groups with cost-effectiveness ratios below the threshold while withholding coverage for the remaining groups would perhaps not pass most tests of equity and not represent a sound application of the threshold. This raises the

question of whether there is a better threshold than $129,090 per QALY. One could even argue that a single "best" threshold that works with all applications is elusive and that differential thresholds may be needed for different subgroups. Just as there are various notions of equity—some of which work better than others in certain circumstances, the choice of threshold must begin with a well-defined notion of equity.

One way of deriving an equitable threshold is to start with the Rawlsian principle of justice: resources should be allocated to benefit everyone, including the most vulnerable individuals [24]. Then, from Figure 2, we can obtain a probabilistic view of the Rawlsian principle: the (100-α)-th percentile of the incremental cost-effectiveness ratio for dialysis can be used as a threshold (i.e., $\alpha = 5$, 10, or 15), with the recognition that this the least of what the threshold needs to be to ensure comparable coverage for the medical intervention in question as for the most expensive α-percent of dialysis patients. Although in a strict sense, the Rawlsian principles would ask that α be set at 0 (i.e. for the society's least fortunate), doing so would not be financially feasible in practice. The laws of randomness would ensure that one can always find some person who observes an arbitrarily poor (high) incremental cost-effectiveness ratio, as is shown in the right asymptote of Figure 2. A reasonable way to "amend" the Rawlsian notion of justice in a world of stochasticity is, therefore, to think of the incremental cost-effectiveness ratio in terms of the tail distribution. In short, the wide distribution of ICER obtained in our analysis shows that there is no single appropriate threshold, but rather a continuum of thresholds, which might be conceptually thought of as a function in α. Thresholds corresponding to smaller values of α reflect a higher emphasis on the distributive implications of the Rawlsian ideal, but also generate a greater financial burden. The decision-maker is confronted with having to make a tradeoff.

One would be naive to expect that a threshold-based system provide the solution to the problem of increasing health-care costs. As the dialysis figures indicate, the threshold can creep higher over time, implying that the amount paid for a fixed increase in quality-adjusted life expectancy may increase over time. Nevertheless, it does provide a heuristical framework where both the cost and effectiveness of a technology is assessed, and more importantly, it can provide incentives for innovators to develop solutions that might reduce the cost of care without adversely affecting the quality of care or life expectancy.

This analysis has several strengths. The USRDS registry includes the vast majority (approximately 95%) of all persons in the United States requiring dialysis and transplantation for ESRD, so that the dialysis results described here are generalizable to the US dialysis population. Moreover, we were able to simulate changes in practice (e.g., long delays in dialysis initiation) that could not be tested in clinical practice. Data from USRDS were supplemented with data from a large integrated health-care delivery system, incorporating information on hospitalization and outcomes that would otherwise be unavailable from the nonelderly and disabled dialysis population without Medicare as primary payer. We have previously validated the simulation model, which yielded results under the Current Practice strategy virtually identical to empirically observed outcomes [9]. Unlike many other medical technologies recently introduced, dialysis has a more than 30-year history of use in the United States, and information on costs and outcomes associated with dialysis and transplantation are more granular than those available for many other high-cost technologies. The estimates of utility were recently obtained, using two conventional, yet disparate measures, which bracketed the model's utility inputs.

The analysis has several limitations. The model does not capture all comorbidities and cannot describe physiological effects or psychosocial factors that might influence the outcomes of care. Using simulation, we cannot determine the exact QALYs and costs. We tried to control for the margin of error in the estimates of QALYs and costs by simulating large populations. In doing so, we were able to reduce the standard error of the estimates to <0.005 QALYs and <$300 lifetime costs.

Arguably, there are more important limitations related to the conclusions that we have drawn from our work. That dialysis reflects an accepted social willingness to pay depends on the assumption that the public and policymakers still believe that dialysis should be provided to all Americans who require it. The decision to provide dialysis as a covered benefit under the Medicare Program in July 1973 was made on the basis of medical justification and political will, with the expectation that many beneficiaries would regain health and return to the workforce [25,26]. Although coverage decisions for new technologies are made with regularity, the decision to approve a new technology has different implications than a decision to withdraw a technology after the latter has been approved and available for decades. Thus, it is possible that the $129,090 per QALY ($61,294 per year) figure for the value of life that we have calculated overestimates the marginal value that might be determined using assessments based on other, newer technologies.

All of the methods for deriving a threshold presented here are based on directly calculating the ICER. A limitation of this approach is that there are many ways to calculating the ICER (as we showed in Table 4). Depending on the point of reference chosen, the results generally differ. This reflects the roots of CEA as an approximation to an underlying optimization problem: there are many ways to construct an approximation. Alternatively, a threshold can also be derived directly from the underlying optimization problem. That approach is conceptually more sophisticated and requires more technical machinery, but it has the appeal of leading to one unambiguous threshold (with a precise mathematical interpretation). The high-level idea there is to set up the current allocation (as represented by Current Practice) as the result of a formal optimization problem with unknown parameters, and iteratively, the unknown parameters are calculated. One of the parameters is a value threshold, and thus it can be viewed as the value threshold *implied* by the current practice of dialysis. Another appeal of that approach is that it provides an exploratory framework for assessing the degree of inequity currently in the system. A downside is that the approach is computationally intensive (relying on methods of inverse optimization), which prevents more casual uses. We discuss that approach in [27].

In summary, using data from the USRDS and other sources, we have determined the cost-effectiveness of dialysis in the modern era. In doing so, based on the assumption that dialysis is a desired benefit to be provided to persons with ESRD, we have determined an empiric value of life. Based on careful simulation, and philosophical principles aimed to protect the vulnerable, we have determined range of dialysis-based thresholds based the tail distribution. Although no method can definitively determine the actual value an individual places on his or her lifetime, these estimates are less prone to some of the problems faced by estimates using labor market data or personal choices involving small but finite risks, which have been shown that people tend to overestimate [28]. Whether these estimates will be used to generate policy decisions remains to be determined.

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